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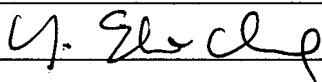
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PRE-APPEAL BRIEF REQUEST FOR REVIEWDocket Number (Optional)
02-1031-A

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name Yijian Elaine ChangApplication Number
10/673,054Filed
September 26, 2003First Named Inventor
Laurie EngelArt Unit
1645Examiner
Vanessa L. Ford

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).

Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)
- ☐ attorney or agent of record.

Registration number _____

- ☒ attorney or agent acting under 37 CFR 1.34.

Registration number if acting under 37 CFR 1.34 54,698

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Typed or printed name

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Telephone number

April 30, 2007

Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☒ *Total of 1 forms are submitted.

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

(Our Case No. 02-1031-A)

In re Application of: Engel, et al.

Serial No.: 10/673,054

Filed: September 26, 2003

For: Cell Lysis Composition, Method of Use,
Apparatus, and Kit

Examiner: Vanessa L. Ford

Group Art Unit: 1645

Confirmation No. 1228

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REASONS FOR PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicant requests review of the Final Office Action mailed January 30, 2007 because the Examiner, when responding to Applicant's arguments, made errors in law.

1. The Claimed Invention

Applicant's claims are directed towards a composition comprising at least one surfactant having a hydrophobic-lipophilic balancing value in the range from about 11 to about 16 and at least one cell membrane altering compound, and kits containing the composition. Claims 1-28, and 125 define each component of the composition. Claims 67-77, 79, and 122-124 are directed to kits for extracting and isolating a protein comprising the composition.

2. Status of the Claims

Claims 1-28, 67-77, 79, and 122-125 are currently pending. Claim 125 has been allowed. Claims 1-28, 67-77, 79, and 122-124 stand rejected on grounds of obviousness over Chu et al. (U.S. Patent No. 6,174,704, "Chu") in view of Shultz et al. (U.S. Patent No. 6,242,235, "Shultz").

3. Clear Legal Deficiency of Rejections

In response to Applicant's argument, Examiner maintained that Chu's disclosure of adding other components that do not adversely affect the use and benefit of the cell lysis solution is a motivation to

combine Chu with Shultz. See page 7 of the Final Office Action of January 30, 2007. Examiner made errors in law because (1) one of skill in the art would not be motivated to combine Chu and Shultz; (2) Examiner did not meet the requirements of Graham analysis in establishing a *prima facie* case of obviousness; and (3) Examiner failed to consider unexpected results of the claimed composition in maintaining the §103(a) rejection.

A. The Examiner failed to establish a *prima facie* case of obviousness because one of skill in the art would not be motivated to combine Chu and Shultz.

The current §103(a) rejection is a result of improper hindsight reconstruction solely based on teachings in the Applicants' disclosure. See pages 9-10 of the March 29, 2007 response (the "3-29-07 response"). Chu merely relates to lysis of host cells and extracting proteins of interest therefrom by employing a solution consisting essentially of an alkylglycoside or alkylthioglycoside. Shultz merely relates to surfactants that stabilize enzyme activities. Contrary to the Examiner's position, there is no teaching or suggestion in Chu that any protein stabilization is necessary or even desirable to do. Indeed, Chu is completely silent with respect to a composition having "at least one surfactant having a hydrophobic-lipophilic balance value in the range from about 11 to about 16" and further in combination with "at least one cell membrane altering compound." That Chu indicates, generally, that other constituents that do not adversely affect the benefits of Chu's solution can be included is merely an invitation to investigate a plethora of compounds. There is nothing in Chu that would provide an ordinary skilled artisan with any motivation to combine Shultz to make the presently claimed composition with the expectation that such composition would provide the surprising and unexpected results discussed below and in the October 30, 2006 response ("10-30-06 response") and the 3-29-07 response. Shultz adds nothing that remedies the deficiencies in Chu's teachings.

Shultz merely relates to compositions for stabilizing proteins, and is limited to cationic surfactants. Moreover, Shultz does not teach or suggest cell lysis nor does he teach or suggest that this would be necessary or desirable to do. On the contrary, some surfactants can form micelles that may make extraction more difficult. Accordingly, without a suggestion of lysis and extraction in Shultz, one of ordinary skill would not be motivated by Shultz's teachings solely concerning protein stabilization to include a surfactant (e.g., Tomah E-18-15 or E-18-5) in Chu's lysis reagent to arrive at the claimed invention with any reasonable expectation of success.

B. The Examiner failed to establish a *prima facie* case of obviousness because the Examiner failed to meet the Graham factual inquiries

Federal case law reiterates the importance of the motivation to combine as a safeguard against impermissible hindsight. See pages 9-11 of the 3-29-07 response. The Supreme Court further set out the factual inquiries in *Graham v John Deere Co.*, 383 U.S. 1, 17 (1966), which the Patent Office must follow in determining obviousness. The Graham factual inquiries were delineated on page 11 of the 3-29-07 response. The Examiner failed to meet the Graham factual inquiries for a *prima facie* case of obviousness as discussed below.

(1) The Scope and Content of the Cited References

Chu merely relates to lysis of host cells and extracting proteins of interest therefrom. Specifically, Chu employs a reagent solution consisting essentially of an alkylglycoside or alkylthioglycoside. However, there is no teaching or suggestion in Chu that any protein stabilization is necessary or even desirable to do. Shultz merely relates to compositions for stabilizing proteins, and is limited to cationic surfactants. Moreover, Shultz does not teach or suggest cell lysis or protein extraction nor does he teach or suggest that this would be necessary or desirable to do.

(2) The Differences Between the Cited References and the Claims

The present claims are directed to cell lysis composition comprising at least one surfactant having hydrophilic-lipophilic balance value in the range from about 11 to about 16 and at least one cell membrane altering compound. Claims 2, 3, 6-12, 16-28, and 125 further define different components of the composition. Claims 67-77, 79, and 122-124 are directed to kits containing the composition. The present claims, considered as a whole, differ from cited art in that Chu does not teach or suggest a surfactant for effective cell lysis. As such, Chu does not provide any kind of motivation to combine Shultz to arrive at the claimed composition.

(3) Level of Ordinary Skill in the Pertinent Art

Both Chu and Shultz are at least of the level of ordinary skill in the art, yet the claimed invention did not occur to either one of them. Nothing in Chu or Shultz provides a motivation to combine the references to arrive at the claimed composition. Additionally, there is nothing implicit in the knowledge of one of ordinary skill in the art to motivate the combination of Chu and Shultz to arrive at the claimed invention.

(4) Evidence of Secondary Consideration

Applicants have submitted unexpected results as evidence of secondary consideration in the 10-30-06 response and the 03-29-07 response. However, the Examiner failed to consider the patentability based on the entire record as discussed below.

C. The claimed invention is not obvious over cited art because the claimed composition produces unexpected results that the Examiner failed to properly consider.

The instant application discloses the results of the levels of a reporter protein (luciferase) released from cells lysed by a cell membrane altering compound alone, by at least one surfactant alone, and by the combination of the two. Chu discloses the use of a cell membrane altering compound to lyse the cell. Shultz discloses the use of a surfactant to stabilize protein activity for enzyme reaction or long term storage. The Applicants had unexpectedly discovered that cell lysis composition containing both a cell membrane altering compound and a surfactant produced a synergistic effect much greater than that obtained with each reagent alone. See pages 9-11 of the 10-30-06 response and pages 12-14 of the 3-29-07 response.

Applicant has demonstrated that the combination of a cell membrane altering compound polymyxin B, and a surfactant, such as Tomah E18-15 or Rhodameen, dramatically increases the release of luciferase from cell debris to the supernatant. See Table A of the 3-29-07 response. The unexpected synergistic effect of the combination results in at least a 178 fold increase in the percentage of luciferase released to the supernatant, comparing to the percentage of luciferase released by polymyxin B alone, Tomah E18-15 alone, or Rhodameen alone.

Even if, for the sake of argument only, there is any suggestion in Chu to include a protein stabilizing agent such as surfactant in a cell lysis composition, it does not follow that the unexpected results obtained from the claimed composition could have been anticipated by one of skill in the art. The test of obviousness is whether the invention as a whole would be obvious, including the nature of the results obtained. The court has stressed that in determining obviousness of the claimed product, the inquiry must not focus solely on the product created, but also on the obviousness or nonobviousness of its creation. *General Motors Corp. v. U. S. International Trade Commission*, 687 F.2d 476, 482-83 (C.C.P.A. 1982). The court's rationale of allowing the use of unexpected results to rebut a *prima facie* case of obviousness is explained on page 12 of the 3-29-07 response. Neither Chu nor Shultz recognizes the synergistic effect of the combination of a cell membrane altering compound and surfactant on cell lysis and protein extraction. Neither Chu nor Shultz appreciates the claimed invention. One of skilled in the art would have found the synergistic effect on cell lysis surprising and unexpected, and thus would have found the invention non-obvious. The Examiner, however, failed to properly consider the unexpected results in maintaining the obviousness rejections. See pages 7-8 of the Final Office Action.

First, a determination under §103 should rest on all evidence and should not be influenced by any earlier conclusion. MPEP 2144.08 III. (emphasis original) The ultimate determination on patentability is

made on the entire record. MPEP 2141 III. Instead of reconsidering the rejection in view of the entire record, however, the Examiner simply asserts that "the composition obtained by the prior art teachings would have the same unexpected characteristics as the claimed composition." See page 7 of the Final Office Action. The assertion is precisely the product of impermissible hindsight reconstruction. Certainly, in hindsight there exists a route to a particular result. However, the disclosure in Chu or Shultz, alone or in combination, in no way foresees the unexpected results obtained by the claimed composition.

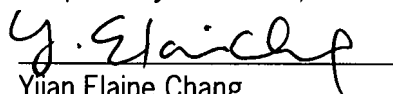
Second, the Court has made it clear that "the inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." *In re Spormann*, 150 U.S.P.Q. 449, 452 (C.C.P.A. 1966) (emphasis added). The unexpected synergistic effect was previously unknown. The Examiner has not provided any basis in fact or technical reasoning indicating that the advantage illustrated by the unexpected results was known to one of skill in the art at the time of the invention, or is taught or suggested by the cited art. The Federal Circuit has explicitly rejected the retrospective view of inherency, as employed by the Examiner, as a substitute for some teaching or suggestion supporting an obviousness rejection. See *In re Rijckaert*, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993). Such a retrospective view of inherency would completely forestall any use of unexpected results as evidence to rebut an obviousness rejection, the use of which has been explicitly sanctioned by the Supreme Court. See *U.S. v. Adams*, 383 U.S. 39, 51-42 (1966). Applicants submit that Examiner has failed to establish a *prima facie* case of obviousness because the Examiner failed to properly consider the evidence of secondary consideration as required by the Graham analysis.

4. Conclusion

For the foregoing reasons, Applicants respectfully submit that all of the pending claims should be allowed.

Date: April 30th, 2007

Respectfully submitted,


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